



# UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE  
United States Patent and Trademark Office  
Address: COMMISSIONER FOR PATENTS  
P.O. Box 1450  
Alexandria, Virginia 22313-1450  
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/780,897	02/19/2004	Mathew Vadas	229752002600	9067
25227 7590 01/31/2007 MORRISON & FOERSTER LLP 1650 TYSONS BOULEVARD SUITE 300 MCLEAN, VA 22102			EXAMINER ROYDS, LESLIE A	
			ART UNIT	PAPER NUMBER
			1614	
SHORTENED STATUTORY PERIOD OF RESPONSE		MAIL DATE	DELIVERY MODE	
3 MONTHS		01/31/2007	PAPER	

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

TH

# Office Action Summary

Application No.

10/780,897

Applicant(s)

VADAS ET AL.

Examiner

Leslie A. Royds

Art Unit

1614

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 16 November 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-37 is/are pending in the application.
- 4a) Of the above claim(s) 32-35 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-31, 36 and 37 is/are rejected.
- 7) ☒ Claim(s) 20 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

## Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

## Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)          | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

### DETAILED ACTION

#### Claims 1-37 are presented for examination.

Acknowledgement is made of the present application as a continuation-in-part (CIP) application of U.S. Patent Application No. 10/275,686, filed June 25, 2003, and claims priority under 35 U.S.C. 119(e) to U.S. Provisional Patent Application No. 60/447,707, filed February 19, 2003. Acknowledgement is also made of Applicant's claims for priority under 35 U.S.C. 119(a-d) to Australian Patent Application No. 2003900729, filed February 19, 2003, of which a certified copy was filed June 28, 2004.

Applicant's Preliminary Amendment filed February 19, 2004 has been received and entered into the application. Accordingly, the specification at page 1 has been amended, claims 1-35 are also amended and claims 36-37 are newly added.

Applicant's Amendment filed August 30, 2004 has also been received and entered into the application. Accordingly, the abstract has been added.

Applicant's response filed November 17, 2006 to the requirement for restriction/election dated May 18, 2006 has been received and entered into the present application.

#### *Requirement for Restriction/Election*

Applicant's election without traverse of the invention of Group I (claims 1-31 and 36-37), directed to a method for modulating the growth of a cell or a method for the treatment and/or prophylaxis of a condition characterized by aberrant, unwanted or otherwise inappropriate cell growth in a mammal, by administering an effective amount of an agent for a time and under conditions sufficient to modulate the functional activity of sphingosine kinase, in the reply filed November 17, 2006, is acknowledged by the Examiner.

Therefore, for the reasons above and those made of record at pages 2-6 of the previous Office

Art Unit: 1614

Action dated May 18, 2006, the election requirement is deemed proper and is made **FINAL**.

Claims 32-35 are **withdrawn** from further consideration pursuant to 37 C.F.R. 1.142(b), as being drawn to non-elected inventions.

The claims corresponding to the elected subject matter are claims 1-31 and 36-37 and such claims are herein acted on the merits.

*Objection to the Claims*

Claim 20 is objected to for failing to conclude with a period.

*Claim Rejections - 35 USC § 112, First Paragraph, Written Description Requirement*

*(New Grounds of Rejection)*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-13, 16-28 and 31 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Present claims 1 and 2 are directed to methods for modulating the growth of a cell comprising contacting said cell with an effective amount of an agent for a time and under conditions sufficient to modulate the functional activity of sphingosine kinase. Present claims 16 and 17 are directed to a method for the treatment or prophylaxis of a condition characterized by aberrant, unwanted or otherwise inappropriate cell growth in a mammal, comprising administering to said mammal an effective amount of an agent for a time and under conditions sufficient to modulate the functional activity of sphingosine

Art Unit: 1614

kinase.

In particular, the specification as originally filed fails to provide adequate written description for the claim limitation(s) directed to the genus of agents capable of modulating the functional activity of sphingosine kinase (i.e., either up-regulation or down-regulation).

Regarding the requirement for adequate written description of chemical entities, Applicant's attention is directed to the MPEP §2163. In particular, *Regents of the University of California v. Eli Lilly & Co.*, 119 F.3d 1559, 1568 (Fed. Cir. 1997), *cert. denied*, 523 U.S. 1089, 118 S. Ct. 1548 (1998), holds that an adequate written description requires a precise definition, such as by structure, formula, chemical name, or physical properties, "not a mere wish or plain for obtaining the claimed chemical invention." *Eli Lilly*, 119 F.3d at 1566. The Federal Circuit has adopted the standard set forth in the Patent and Trademark Office ("PTO") Guidelines for *Examination of Patent Applications* under the 35 U.S.C. 112.1 "Written Description" Requirement ("*Guidelines*"), 66 Fed. Reg. 1099 (Jan. 5, 2001), which state that the written description requirement can be met by "showing that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics," including, *inter alia*, "functional characteristics when coupled with a known or disclosed correlation between function and structure..." *Enzo Biochem, Inc. v. Gen-Probe Inc.*, 296 F.3d 316, 1324-25 (Fed. Cir. 2002) (quoting *Guidelines*, 66 Fed. Reg. at 1106 (emphasis added)). Moreover, although *Eli Lilly* and *Enzo* were decided within the factual context of DNA sequences, this does not preclude extending the reasoning of those cases to chemical structures in general. *Univ. of Rochester v. G.D. Searle & Co.*, 249 Supp. 2d 216, 225 (W.D.N.Y. 2003).

Regarding Applicant's limitation directed to an agent capable of modulating the functional activity of sphingosine kinase, Applicant has failed to provide any structural characteristics, chemical formula, name(s) or physical properties, aside from the express identification of the compounds N,N-dimethylsphingosine or DL-threo-dihydrosphingosine, that would provide adequate written description of the genus of agents capable of modulating the functional activity of sphingosine kinase that Applicant

Art Unit: 1614

was actually in possession of, and intended to be used within the context of the present invention, at the time of the present invention.

Applicant's specification states at page 15, lines 8-21, "The present invention contemplates chemical analogs of said sphingosine kinase capable of acting as agonists or antagonists of said sphingosine kinase. Chemical agonist may not necessarily be derived from said sphingosine kinase but may share certain conformational similarities. Alternatively, chemical agonists may be specifically designed to mimic certain physiochemical properties of said sphingosine kinase. Antagonists may be any compound capable of blocking, inhibiting or otherwise preventing said sphingosine kinase from carrying out its normal biological functions (for example, N,N-dimethylsphingosine or DL-threo-dihydrosphingosine). Antagonists include monoclonal antibodies specific for said sphingosine kinase, or parts of said sphingosine kinase, and antisense nucleic acids which prevent transcription or translation of genes or mRNA in the subject cells. Modulation of expression may also be achieved utilizing antigens, RNA, ribosomes, DNazymes, RNA aptamers, antibodies or molecules suitable for use in co-suppression." Applicant further exemplifies the use of N,N-dimethylsphingosine at pages 34-40.

Such disclosure, while noted, provides only an exemplary and non-limiting teaching of what agents that would be considered within the scope of the term "agents capable of modulating the functional activity of sphingosine kinase". Applicant has failed to provide any limiting definition or any chemical or physical characteristics of these agents such that one of ordinary skill in the art would have been able to readily identify the scope of those compounds encompassed by the term "agents capable of modulating the functional activity of sphingosine kinase".

MPEP §2163 recites, "The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed

Art Unit: 1614

correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the Applicant was in possession of the claimed genus.” Please reference *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406.

Further, Applicant has failed to define any structural component, such as a common core structural element, as being responsible for the function of the compound as a modulator of the functional activity of sphingosine kinase and, thus, has failed to define the metes and bounds of the genus. In the absence of such boundaries, the very genus of agents capable of modulating the functional activity of sphingosine kinase reads upon thousands, if not millions, of different compounds that meet this functional limitation, though many may not have even been in the possession of Applicant at the time of the invention. Additionally, the fact that Applicant states that this genus of agents encompasses organic compounds, as well as antigens, RNA, ribosomes, DNazymes, RNA aptamers, antibodies or other molecules is clearly indicative of substantial variation within the genus of compounds that are capable of modulating the function of sphingosine kinase. In accordance with the written description requirement of 35 U.S.C. 112, first paragraph, substantial variation that exists within a large and highly varied genus of compounds requires at least a description of a representative number of species of the genus in order to satisfy the requirement, of which Applicant has only provided two such species.

It has been held that when there is substantial variation within a genus that one must describe a sufficient variety of species to reflect the variation within the genus. Given that Applicant has placed no limitation on the identity of the compounds with the genus of “agents capable of modulating the functional activity of sphingosine kinase”, the disclosure of two species fails to represent a variety of species that would reflect the substantial variation inherently present within the genus. Accordingly, the disclosure fails to demonstrate that Applicant was actually in possession of the entire genus of agents capable of modulating the activity of sphingosine kinase.

While it is duly noted that the genus of agents capable of modulating sphingosine kinase activity

Art Unit: 1614

is limited to those capable of functioning in this manner, it remains that Applicant has not appropriately defined the metes and bounds of the genus, even when limited by function (step-plus-function form). MPEP §2163 teaches that step-plus-function claims are adequately described if “the written description *adequately links or associates adequately described particular structure, material, or acts to the function recited in a step-plus-function claim limitation,*” or if “it is clear based on the facts of the application that one skilled in the art would have known what structure, material, or acts perform the function recited in a step-plus-function limitation.” The instant application does not meet either of these criteria. The present specification provides no disclosure beyond the two exemplary agents that would provide a means for identifying compounds, other than those specifically disclosed by Applicant, that would have been amenable for use in the present invention, nor does it specifically teach a common structural elements that performs the function recited in the claim and would be readily identifiable to one of skill in the art. Furthermore, it has been held that a wish or plan for obtaining the chemical invention as claimed does not provide adequate written description of a chemical invention. Rather, a precise definition, such as by structure, formula, chemical name or physical properties or a combination thereof, is required. Please reference, e.g., *Univ. of Rochester v. G.D. Searle & Co.*, 358 F.3d 916, 927, 69 USPQ2d 1886, 1894-95 (Fed. Cir. 2004).

While it is recognized that adequate written description of a limitation is not required to be stated *in haec verba* in the specification or claims as originally filed, adequate written support for claim limitations must arise from either an explicit or implicit suggestion by the disclosure to show that such a concept as claimed was actually in possession of Applicant at the time of the invention. For the reasons provided *supra*, Applicant has failed to provide the necessary teachings, by describing the claimed invention with all of its limitations using such descriptive means that fully set forth the claimed invention, in such a way as to reasonably convey to one skilled in the relevant art that Applicant had possession of the entire genus of agents capable of modulating the functional activity of sphingosine kinase.



Art Unit: 1614

Accordingly, the claims are considered to lack sufficient written description and are properly rejected under 35 U.S.C. 112, first paragraph.

Claims 16-31 and 36-37 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Present claims 16 and 17 are directed to a method for the treatment or prophylaxis of a condition characterized by aberrant, unwanted or otherwise inappropriate cell growth in a mammal, comprising administering to said mammal an effective amount of an agent for a time and under conditions sufficient to modulate the functional activity of sphingosine kinase.

In particular, the specification as originally filed fails to provide adequate written description for the genus of conditions characterized by aberrant, unwanted or otherwise inappropriate cell growth (claims 16 and 17).

MPEP §2163 states, "The issue of a lack of adequate written description may arise even for an original claim when an aspect of the claimed invention has not been described with sufficient particularity such that one skilled in the art would recognize that the applicant had possession of the claimed invention. The claimed invention as a whole may not be adequately described if the claims require an essential or critical feature which is not adequately described in the specification and which is not convention in the art or known to one of ordinary skill in the art...The courts have described the essential question to be addressed in a description requirement issue in a variety of ways. An objective standard for determining compliance with the written description requirement is, "does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed." *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989). Under *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555,

Art Unit: 1614

1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991), to satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention, and that the invention, in that context, is whatever is now claimed. The test for sufficiency of support in a parent application is whether the disclosure of the application relied upon “reasonably conveys to the artisan that the inventor had possession at that time of the later claimed subject matter.” *Ralston Purina Co. v. Far-Mar-Co., Inc.*, 772 F.2d 1570, 1575, 227 USPQ 177, 179 (Fed. Cir. 1985) (quoting *In re Kaslow*, 707 F.2d 1366, 1375, 217 USPQ 1089, 1096 (Fed. Cir. 1983))...Whenever the issue arises, the fundamental factual inquiry is whether the specification conveys with reasonable clarity to those skilled in the art that, as of the filing date sought, applicant was in possession of the invention as now claimed. See, e.g., *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991).”

Applicant states at page 29, lines 4-8, “Reference to ‘aberrant, unwanted or otherwise inappropriate’ cell growth should be understood as a reference to over active cell growth, to physiologically normal cell growth which is inappropriate in that it is unwanted or to insufficient cell growth. Preferably, said inappropriate cell growth is uncontrolled cell proliferation induced by sphingosine kinase overexpression.”

However, Applicant has only provided the exemplary condition of neoplastic or malignant cancers as a condition representative of the genus of disorders associated with aberrant, unwanted or otherwise inappropriate cell growth, but has failed to provide any limiting definition of the genus of disorders associated with aberrant, unwanted or otherwise inappropriate cell growth that Applicant was in possession of, and intended to be treated using the presently claimed agent(s), at the time of the invention. In other words, Applicant has failed to define this genus of disorders in such a manner as to provide adequate written description of the full scope of the claimed genus.

Applicant merely requires that the disorder being treated is associated with, or characterized by,

Art Unit: 1614

aberrant, unwanted or inappropriate cell growth, but fails to objectively define what is meant by “unwanted or inappropriate” cell growth such that one of ordinary skill in the art at the time of the invention would have been reasonably apprised of the scope of disorders intended by the claimed genus. Further, the genus of disorders associated with aberrant cell proliferation is large and highly varied, and includes such disparate species, such as, e.g., cancer, psoriasis, fibrotic disorders, atherosclerosis, etc. Given the etiological and pathophysiological variation with the genus of disorders that are characterized by aberrant cell growth, it is clear that the disclosure of a single species (i.e., cancer) is not a reasonably representative set of species. It has been held in patent law that when there is substantial variation within a genus, Applicant is required to describe a sufficient variety of species to reflect the variation within the genus.

As stated in MPEP §2163, “The subject matter of the claim need not be described literally (i.e., using the same terms or *in haec verba*) in order for the disclosure to satisfy the description requirement.” However, considering the teachings provided in the specification as originally filed, Applicant has failed to provide the necessary teachings, by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams and formula that fully set forth the claimed invention, in such a way as to reasonably convey to one skilled in the relevant art that Applicant had possession of the concept of administering the presently claimed agent(s) for the treatment of a condition characterized by aberrant, unwanted or inappropriate cell growth.

Accordingly, the claims are considered to lack sufficient written description and are properly rejected under 35 U.S.C. 112, first paragraph.

***Claim Rejections - 35 USC § 112, First Paragraph, Scope of Enablement***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode

Art Unit: 1614

contemplated by the inventor of carrying out his invention.

Claims 1-31 and 36-37 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for reducing the concentration of Ras-transformed fibroblasts (in which Ras expression is upregulated) by down-regulating the activity of sphingosine kinase (SphK) using dimethylsphingosine or reducing the proliferation of human breast adenocarcinoma cells by down-regulating the expression of SphK using dimethylsphingosine, does not reasonably provide enablement for the modulation of the growth of any cell, in particular, any malignant neoplastic cell, using any agent that modulates the functional activity of SphK, nor does the specification reasonably provide enablement for the treatment or prophylaxis of any condition characterized by aberrant, unwanted or inappropriate cell growth, particularly, particularly malignant neoplasm. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with the claims.

In this regard, the application disclosure and claims have been compared per the factors indicated in the decision *In re Wands*, 8 USPQ 2d 1400 (Fed. Cir., 1988) as to undue experimentation. The factors include:

- 1) the nature of the invention;
- 2) the breadth of the claims;
- 3) the predictability or unpredictability of the art;
- 4) the amount of direction or guidance presented;
- 5) the presence or absence of working examples;
- 6) the quantity of experimentation necessary;
- 7) the state of the prior art; and,
- 8) the relative skill of those skilled in the art.

The relevant factors are addressed below on the basis of comparison of the disclosure, the claims and the state of the prior art in the assessment of undue experimentation.

For the purposes of examination under 35 U.S.C. 112, first paragraph, the rejection will be set forth insofar as it reads upon the treatment of neoplastic cells or cancer(s). The same reasoning applies to

Art Unit: 1614

the treatment of other cell types or other conditions characterized by aberrant, unwanted or inappropriate cell growth, but for the obvious difference in the type of disorder.

The presently claimed invention is directed to methods for modulating the growth of a cell comprising contacting said cell with an effective amount of an agent for a time and under conditions sufficient to modulate the functional activity of sphingosine kinase (see, e.g., claims 1-2), as well as methods for the treatment or prophylaxis of a condition characterized by aberrant, unwanted or otherwise inappropriate cell growth in a mammal, comprising administering to said mammal an effective amount of an agent for a time and under conditions sufficient to modulate the functional activity of sphingosine kinase (see, e.g., claims 16-17).

In particular, one skilled in the art could not practice the presently claimed subject matter without undue experimentation because the artisan would not accept on its face that the treatment of any neoplastic cell or cancer type could be effectively achieved by the administration of any agent capable of modulating the activity of SphK. Based upon the state of the art, as discussed below, the artisan would have only accepted that the treatment of specific neoplastic cell or cancer types, such as Ras-transformed fibroblasts or human breast adenocarcinoma, could be achieved with the compound dimethylsphingosine, identified as having activity in treating such cells or cancer.

As set forth in *In re Marzocchi et al.*, 169 USPQ 367 (CCPA 1971):

“[A] [s]pecification disclosure which contains the teachings of manner and process of making and using the invention in terms corresponding to the scope to those used in describing and defining subject matter sought to be patented must be taken as in compliance with the enabling requirement of first paragraph of 35 U.S.C. 112 *unless there is reason to doubt the objective truth of statements contained therein which must be relied on for enabling support*; assuming that sufficient reasons for such doubt exists, a rejection for failure to teach how to make and/or use will be proper on that basis, such a rejection can be overcome by suitable proofs indicating that teaching contained in the specification is truly

Art Unit: 1614

enabling.” (emphasis added)

The present claims circumscribe a method of treating any type of neoplastic cell or treating or preventing any type of cancer by administering or applying any agent capable of modulating the activity of SphK. That is, in order to be enabled to practice the present invention, the skilled artisan would have to accept that by administering any agent capable of modulating the function of SphK, any neoplastic cell or any cancer known in the art could be reasonably treated, or even prevented. In light of the fact that the specification not only fails to provide the skilled artisan with any direction or guidance as to how the treatment of any neoplastic cell or cancer or the prevention of any cancer could actually be achieved using the claimed genus of agents capable of modulating SphK activity, but also fails to direct the skilled artisan as to (1) what other agents other than dimethylsphingosine would be capable of modulating SphK activity or (2) which other neoplastic cell or cancer types would be sensitive to this chemotherapeutic approach and how one would determine such sensitivity, and especially in light of the highly complex nature of tumors and cancer in general, the specification, which lacks an objective showing of which other neoplastic cells or cancers could be effectively treated using the claimed SphK modulating agent(s) and which other SphK modulating agent(s) would be effective for achieving such an objective, is viewed as lacking an enabling disclosure of the entire scope of the claimed invention.

Here, the objective truth that any neoplastic cell or cancer type may be treated with the claimed SphK modulating agent is doubted because, while the state of the art of cancer treatment is well developed with regard to the treatment of specific cancer types with specific chemotherapeutic regimens (see Cecil's Textbook of Medicine, pages 1060-1074), the state of the art with regard to treating all cancers using a single agent or preventing all cancers using a single agent is grossly underdeveloped.

In this regard, Cecil's Textbook of Medicine (2000) is cited. In particular, there is no known anticancer agent or combination of anticancer agents that is effective against treating all cancer types, or is there any known anticancer agent or combination of agents that is effective against inhibiting the

Art Unit: 1614

growth of any type of cancer cell. The Cecil reference clearly shows that for the various known cancer types, there is not one specific chemotherapeutic agent or combination thereof that is effective at treating cancer or inhibiting the growth of cancer cells for each and every type of cancer (see Table 198-5 at page 1065; Tables 198-6 and 198-7 at pages 1066; Table 198-8 at page 1068; and Table 198-9 at page 1071).

Given that there was not known any specific agent or combination of agents or genus of agents with a common functional activity effective to treat, let alone prevent, all known types of cancer, one of ordinary skill in the art would not accept on its face Applicant's statement that such an objective could be achieved in any type of neoplastic cell or tumor using the presently claimed genus of agents capable of modulating SphK without enabling a set of species at least representative of the full scope of cancers known in the art. Further, one of ordinary skill in the art would also not accept on its face Applicant's statement that such an objective could be achieved using any agent capable of modulating SphK, particularly since Applicant has failed to define the agents that would be encompassed by such a genus, and further in the absence of at least an enabling disclosure of a set of species at least representative of the full scope of agents with this function.

The artisan would have required sufficient direction as to how, at minimum, a representative set of species of cancer would be effectively treated with a representative set of species of agent capable of modulating SphK and, further, how the artisan could have reasonably extrapolated such results to the larger and highly varied genus of cancers in general or SphK modulating agents in general without requiring undue experimentation to determine (1) what types of cancer would actually show sensitivity to the presently claimed SphK modulating agents or (2) what types of SphK modulating agents would actually have activity in treating such cancers, such that the artisan would have been imbued with at least a reasonable expectation of success in treating, let alone preventing, the cancer. Such success would not have been reasonably expected for all cancers claimed given the highly complex and variable nature of all cancers known in the art and that Applicant has shown an example in human breast adenocarcinoma or

Art Unit: 1614

oncogenic fibroblasts. To the artisan, the concept of a single agent or single genus of functional agents to treat two specific cell types would not have been considered representative or suggestive of the same efficacy in the treatment of all known cancer types in the absence of any evidence or reasoning to do so. Additionally, since the skilled artisan would have expected the interaction of a particular agent in the treatment of a particular disease state to be very specific and highly unpredictable absent a clear understanding of the structural and biochemical basis for the use of each agent, one of skill in the art would have no other recourse but undue experimentation to undertake extensive testing to determine which other cancer types or which other SphK modulating agents could be used in the claimed method(s).

It is in this regard that Applicant is directed to the MPEP at §2164.08. All questions of enablement are evaluated against the claimed subject matter. Concerning the breadth of a claim relevant to enablement, the only relevant concern is whether the scope of enablement provided to one skilled in the art by the disclosure is commensurate with the scope of protection sought by the claims. The determination of the propriety of a rejection based upon the scope of a claim relative to the scope of enablement involves the determination of how broad the claim is with respect to the disclosure and the determination of whether one skilled in the art is enabled to use the *entire scope* of the claimed invention without undue experimentation.

A conclusion of a lack of enablement must take into consideration the unpredictability in the art at the time of the invention and the direction or guidance provided by Applicant. The amount of guidance required to be present in the specification as originally filed is directly proportional to the amount of knowledge in the art as well as the unpredictability in the art. In other words, if little or nothing is known in the prior art about an aspect of the claimed invention and the art is unpredictable, the specification needs more detail and guidance as to how to use the invention in order to be enabling. Please reference *In re Fisher*, 417 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) and *Chiron Corp. v. Genentech Inc.*, 363 F.3d 1247, 1254, 70 USPQ2d 1321, 1326 (Fed. Cir. 2004).



The enablement of the working examples provided in the specification is not disputed. However, they are not representative of the breadth of the presently claimed subject matter. Applicant's claims broadly claim the use of any agent capable of modulating SphK for use in treating any neoplastic cell or cancer type or preventing any cancer type. The fact that Applicant has exemplified the use of a single SphK modulating agent (i.e., dimethylsphingosine) in human breast adenocarcinoma or oncogenic fibroblasts does not address the high degree of variability in the art in terms of the pathophysiological differences among tumor types and their reactivity to different anticancer compounds and also the variability in function that would necessarily result from the different chemical and structural properties of pharmaceutical agent(s). Applicant has also failed to provide any evidence, or describe any protocol, that addresses this variability in the art such that one of ordinary skill in the art would have been imbued with at least a reasonable expectation of success in treating any neoplastic cell or cancer type or preventing any cancer type using any SphK modulating agent based on the direction provided in the present specification. While the lack of a working embodiment cannot be the sole factor in determining enablement, the absence of substantial evidence commensurate in scope with the presently claimed subject matter, in light of the unpredictable nature of the art and the direction that Applicant has presented, provides additional weight to the present conclusion of insufficient enablement in consideration of the *Wands* factors as a whole.

For example, the term "solid tumor" alone encompasses three distinctly different categories of tumors: (1) sarcomas, those that arise from connective or supporting tissues, such as bone or muscle; (2) carcinomas, those that arise from glandular tissues and epithelial cells; and (3) lymphomas, those that arise from the lymphoid organs, such as the lymph nodes, spleen or thymus. Though each of these three types can be lumped under the umbrella category of "solid tumor", the distinct etiology and pathophysiological differences between these three categories of solid tumor would not have imbued the skilled artisan with a reasonable expectation of success in treating any one or more of these types of solid

Art Unit: 1614

tumor when efficacy had only been demonstrated in a single breast cell line or a single oncogene-transformed fibroblast line.

In light of such, it is clear that one of ordinary skill in the art would be faced with the impermissible burden of undue experimentation in order to execute the entire scope of the subject matter presently claimed. The basis for the present rejection is not simply that experimentation would be required, since it is clear from the state of the pharmaceutical and chemical arts that experimentation in this particular art is not at all uncommon, but that the level of experimentation required in order to practice this aspect of the invention in the absence of any enabling direction by Applicant would be *undue*. Please reference *In re Angstadt*, 537 F.2d 498, 504, 190 USPQ 214, 219 (CCPA 1976), which states, "The test of enablement is not whether any experimentation is necessary, but whether, *if experimentation is necessary, it is undue*." (emphasis added) Given the high degree of unpredictability noted and recognized in the art with regard to the treatment of tumors, the state of the art clearly precludes the general extrapolation of the results seen in two tumor types to the larger and much more highly varied genus of tumors as a whole. In the absence of any direction or guidance presented by Applicant as to how such a therapeutic objective could be achieved without necessitating an undue level of experimentation, the present disclosure is viewed as lacking an enabling disclosure of the *entire scope* of the presently claimed subject matter.

In view of the discussion of each of the preceding seven factors, the level of skill in the art is high and is at least that of a medical doctor with several years of experience in the art.

As the cited art and discussion of the above factors establish, practicing the claimed method in the manner disclosed by Applicant would not imbue the skilled artisan with a reasonable expectation that the use of any SphK modulating agent would have necessarily had efficacy in the treatment of any neoplastic cell or cancer type or in the prevention of any cancer type. In order to actually achieve such a result, it is clear from the discussion above that the skilled artisan could not rely upon Applicant's disclosure as

Art Unit: 1614

required by 35 U.S.C. 112, first paragraph, and would have no alternative recourse but the impermissible burden of undue experimentation in order to practice the full scope of the presently claimed invention.

*Claim Rejections - 35 USC § 112, Second Paragraph*

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-31 and 36-37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

Present claims 1 and 2 are directed to methods for modulating the growth of a cell comprising contacting said cell with an effective amount of an agent for a time and under conditions sufficient to modulate the functional activity of sphingosine kinase. Present claims 16 and 17 are directed to a method for the treatment or prophylaxis of a condition characterized by aberrant, unwanted or otherwise inappropriate cell growth in a mammal, comprising administering to said mammal an effective amount of an agent for a time and under conditions sufficient to modulate the functional activity of sphingosine kinase.

In particular, it is noted that present claims 1 and 2 read upon a “method of modulating the growth of a cell”, but Applicant has failed to connect the preamble objective of modulating cell growth to the cell actually being treated by the method. For example, it is not clear whether the cell is actually in need of growth modulation or whether the method is intended for practice in any cell that may or may not need growth modulation. In other words, Applicant has not made clear on the record whether the cell is one in need of growth modulation.

Additionally, present claims 16 and 17 read upon a “method for the treatment or prophylaxis of a condition characterized by aberrant, unwanted to otherwise inappropriate cell growth in a mammal”, but

Art Unit: 1614

Applicant has again failed to connect the preamble objective of treating (prophylactic or otherwise) to the mammal actually being treated by the method. For example, it is not clear whether the mammal is actually in need of treatment of such a condition or whether the method is intended for practice in any mammal that may or may not have such a condition. In other words, Applicant has not made clear on the record whether the subject is one in need of treatment of a condition characterized by aberrant, unwanted or inappropriate cell growth.

Further, Applicant's claims are directed to an effective amount of an agent, which "for a time and under conditions sufficient to modulate the functional activity of sphingosine kinase", is capable of altering the activity of SphK. However, it is unclear as to what the metes and bounds of the limitation "for a time and under conditions sufficient to" is intended to encompass. Specifically, Applicant fails to clearly delineate whether this is a unique amount of time and unique conditions under which the modulation will only occur if such conditions are present and what, in particular, are the actually conditions that are sufficient to effect such a modulation.

For these reasons, the metes and bounds of the present claims cannot be identified and one of ordinary skill in the art would not necessarily be reasonably apprised of the scope of the claims. In light of such, claims 1-31 and 36-37 fail to meet the tenor and express requirements of 35 U.S.C. 112, second paragraph, and are, thus, properly rejected.

Claims 22-31 and 36-37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

Present claim 21 is directed to a method for the treatment or prophylaxis of a condition characterized by aberrant, unwanted or otherwise inappropriate cell growth in a mammal, comprising administering to said mammal an effective amount of an agent for a time and under conditions sufficient

Art Unit: 1614

to modulate the level of functional activity of sphingosine kinase, wherein down-regulation of the functional activity of said sphingosine kinase down-regulates uncontrolled proliferation and functional activity of the kinase. Present claim 22 is directed to a method of the same, wherein said cell is a neoplastic cell.

There is insufficient antecedent basis for the limitation "said cell is a neoplastic cell" in present claim 22, since any reference to such a cell in the claim from which it depends (i.e., claim 21) is noticeably absent. It is unclear how Applicant intends claim 22 to limit the presently claimed subject matter. Additionally, claims 23-31 and 36-37, which are dependent from claim 22, fail to cure this deficiency. As a result, the claims fail to meet the tenor and express requirements of 35 U.S.C. 112, second paragraph, and are, thus, properly rejected for rendering the scope of the claims indefinite.

For the purposes of examination and the application of prior art, present claims 22-31 and 36-37 will be interpreted to read upon the treatment of a neoplastic cancer of the colon, stomach, lung, brain, bone, breast, esophagus or pancreas.

#### *Claim Rejections - 35 USC § 102*

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-10, 13-25, 28-31 and 36-37 rejected under 35 U.S.C. 102(b) as being anticipated by Spiegel (WO 99/61581; 1999).

Spiegel teaches a method for increasing cell proliferation to treat diseases associated with a decrease in sphingosine kinase (SPHK), such as developmental retardation, by administering an agonist of SPHK to stimulate the level of SPHK in the patient (p.38, l.21-27). Spiegel also teaches a method for

Art Unit: 1614

increasing SPHK in a cell by introducing into said cell an SPHK nucleic acid such that said nucleic acid is expressed and SPHK is produced in said cell (p.89, l.4-7), which ultimately results in increased expression of SPHK and, thus, increased cell proliferation (p.5, l.17-21). Spiegel further teaches a method for treating or ameliorating a disease resulting from an increase in cellular proliferation (p.8, l.27-34), such as cancer (p.36, l.22-27), comprising providing to an individual in need of such treatment an effective amount of an antibody against SPHK or an agent that inhibits SPHK expression or function in a pharmaceutically acceptable excipient (p.8, l.27-34), wherein cancers known to express increased levels of SPHK RNA or SPHK protein include lung carcinomas, stomach carcinoma, ovarian carcinoma, pancreatic adenocarcinoma, esophageal carcinoma, brain tumor and bone sarcoma, each of which is known to be predictive of metastatic potential (p.35, l.7-32). Spiegel further teaches the administration of the active compound capable of reducing or inhibiting SPHK via incorporation into a biodegradable polymer and implanted for release at the site of the tumor (p.38, l.2-7). Spiegel defines the amount to be administered as sufficient to "effect" the inhibition or induction of SPHK if the dosage, route of administration, etc. of the agent are sufficient to influence such a response (p.38, l.17-20). Spiegel discloses N,N-dimethylsphingosine and DL-threo-dihydrosphingosine as SPHK inhibitors (p.36, l.12-18).

### *Claim Rejections - 35 USC § 103*

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary.

Art Unit: 1614

Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-31 and 36-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Spiegel (WO 99/61581; 1999) in view of Prashad (U.S. Patent No. 5,068,175; 1991).

Spiegel teaches a method for increasing cell proliferation to treat diseases associated with a decrease in sphingosine kinase (SPHK), such as developmental retardation, by administering an agonist of SPHK to stimulate the level of SPHK in the patient (p.38, l.21-27). Spiegel also teaches a method for increasing SPHK in a cell by introducing into said cell an SPHK nucleic acid such that said nucleic acid is expressed and SPHK is produced in said cell (p.89, l.4-7), which ultimately results in increased expression of SPHK and, thus, increased cell proliferation (p.5, l.17-21). Spiegel further teaches a method for treating or ameliorating a disease resulting from an increase in cellular proliferation (p.8, l.27-34), such as cancer (p.36, l.22-27), comprising providing to an individual in need of such treatment an effective amount of an antibody against SPHK or an agent that inhibits SPHK expression or function in a pharmaceutically acceptable excipient (p.8, l.27-34), wherein cancers known to express increased levels of SPHK RNA or SPHK protein include lung carcinomas, stomach carcinoma, ovarian carcinoma, pancreatic adenocarcinoma, esophageal carcinoma, brain tumor and bone sarcoma, each of which is known to be predictive of metastatic potential (p.35, l.7-32). Spiegel further teaches the administration of the active compound capable of reducing or inhibiting SPHK via incorporation into a biodegradable polymer and implanted for release at the site of the tumor (p.38, l.2-7). Spiegel defines the amount to be administered as sufficient to "effect" the inhibition or induction of SPHK if the dosage, route of administration, etc. of the agent are sufficient to influence such a response (p.38, l.17-20). Spiegel discloses N,N-dimethylsphingosine and DL-threo-dihydrosphingosine as SPHK inhibitors (p.36, l.12-18).

Art Unit: 1614

Though Spiegel fails to expressly teach that the malignant neoplastic cell(s) have been transformed due to the up-regulation of the oncogene Ras, Prashad is cited for its teachings that the cellular oncogene, Ras, is one of the most frequently identified activated oncogenes that results in neoplastic cell growth following transformation from a proto-oncogene to an oncogene via one of the following mechanisms: (1) point mutations in the coding region, (2) amplification of genes or (3) chromosomal translocation. Prashad states, "Activation of ras oncogene causes an increase of ras specific protein (p21) in colon, colorectal, lung, mammary, neuroblastoma, prostate, ovarian, melanoma and bladder carcinomas (references omitted). Thus, one can readily deduce that the p21 ras oncogene protein is a powerful tumor marker." Please see Prashad at col.1, lines 37-58. It is clear from this teaching that it would have been *prima facie* obvious to one of ordinary skill in the art that the colon, lung, brain or breast carcinomas expressly taught by Spiegel would have been reasonably expected to have resulted from the transformation from a physiologically normal cell to a neoplasm due to the up-regulation of Ras, which was well known in the art at the time of the invention to be a tumor marker expressly associated with these specific cancer types.

### *Double Patenting*

#### **Obviousness-Type Double Patenting**

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or



Art Unit: 1614

claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-4, 6-19 and 21-22 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 8-9, 11-15, 29, 49-55 of copending U.S. Patent Application No. 10/275,686.

An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claims because the examined claim is either anticipated by, or would have been obvious over, the reference claims.

Although the conflicting claims are not identical, the copending claims and those of the present application are not considered to be patentably distinct from each other because the copending claims clearly anticipate the present claims. The copending claims clearly provide for methods of downregulating the proliferation of a neoplastic cell, especially wherein the cell is malignant and is from the colon, stomach, lung, brain, bone, esophagus, pancreas, breast, ovary or uterus and had become transformed due to upregulation of the oncogene Ras, comprising contacting the cell with an effective amount of an agent for a time and under conditions sufficient to downregulate the functional activity of SphK, such as, e.g., N,N-dimethylsphingosine or DL-threo-dihydrosphingosine.

Further, the copending claims also clearly provide for methods for the treatment or prophylaxis of a neoplastic cell proliferation condition in a mammal, especially wherein the cell has become transformed due to upregulation of the oncogene Ras, comprising the administration to a mammal, such as, e.g., a human, an effective amount of an agent for a time and under conditions sufficient to downregulate the functional activity of sphingosine kinase, such as, e.g., those species of agents listed in claims 49-55. Though the present claims are directed to the use of the genus of agents capable of downregulating the functional activity of SphK where the copending claims recite particular species of agents capable of this

Art Unit: 1614

function, it has been held in patent law that claims directed to a species will always anticipate a genus. Please reference MPEP §2131.02 for a discussion of genus-species situations and also *In re Slayter*, 276 F.2d 408, 411, 125 USPQ 345, 347 (CCPA 1960) and *In re Gosteli*, 872 F.2d 1008, 10 USPQ2d 1614 (Fed. Cir. 1989).

Accordingly, rejection of present claims 1-4, 6-19 and 21-22 is proper over claims 1, 8-9, 11-15, 29, 49-55 of copending U.S. Patent Application No. 10/275,686 as claiming obvious and unpatentable variants thereof.

Claims 1, 3-6, 16-18, 21-22, 31 and 36-37 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-5, 7 and 18-26 of copending U.S. Patent Application No. 10/531,626.

An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claims because the examined claim is either anticipated by, or would have been obvious over, the reference claims.

Although the conflicting claims are not identical, the copending claims and those of the present application are not considered to be patentably distinct from each other because the copending claims render the present claims obvious. The copending claims clearly provide for the modulation of the proliferation of a cell (i.e., an endothelial cell) via the modulation of the functional level of SphK by inducing over-expression of SphK (see, e.g., copending claims 1-2, 4-5, 7 and 20-26). Though the present claims are directed to the use of the genus of agents capable of downregulating the functional activity of SphK where the copending claims recite particular species of agents capable of this function (see, e.g., claims 20-24), it has been held in patent law that claims directed to a species will always anticipate a genus. Please reference MPEP §2131.02 for a discussion of genus-species situations and also

Art Unit: 1614

*In re Slayter*, 276 F.2d 408, 411, 125 USPQ 345, 347 (CCPA 1960) and *In re Gosteli*, 872 F.2d 1008, 10 USPQ2d 1614 (Fed. Cir. 1989). Further, though the present claims are directed to cells *per se* where the copending claims recite the particular species of endothelial cell, the claims directed to the species of endothelial cell will always anticipate the genus of cells *per se*.

Additionally, the copending claims also clearly provide for the treatment or prophylaxis of a condition characterized by aberrant or unwanted endothelial cell functioning in a mammal via the modulation of the functional level of SphK by inducing over-expression of SphK, particularly wherein the condition to be treated is a tumor (see, e.g., copending claims 3 and 18-19). Though the copending claims do not expressly acknowledge the neoplastic or tumorigenic nature of the cell, nor the specific modulation of the proliferation of the cell, the very teaching of the treatment of a tumor is plainly indicative of the fact that neoplastic cells or tumor cells are present in the host and are, thus, treated according to the claimed method. Further, it is noted that the very teaching of the treatment of a tumor would necessarily affect the proliferation of the tumor cells in order to achieve such a therapeutic objective.

Lastly, though the copending claims do not expressly teach the execution of the claimed method in a human, the practice of such a method in a human would have naturally commended itself to one of ordinary skill in the art at the time of the invention motivated by the desire to treat such neoplastic or tumorigenic conditions in human subjects *per se*.

Accordingly, rejection of present claims 1, 3-6, 16-18, 21-22, 31 and 36-37 is proper over claims 1-5, 7 and 18-26 of copending U.S. Patent Application No. 10/531,626 as claiming obvious and unpatentable variants thereof.

### *Conclusion*

Rejection of claims 1-31 and 36-37 is proper.

Claims 32-35 are withdrawn from consideration pursuant to 37 C.F.R. 1.142(b).

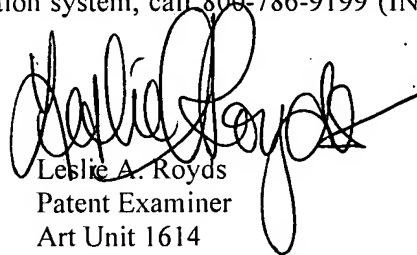
Art Unit: 1614

No claims of the present application are allowed.


Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leslie A. Royds whose telephone number is (571)-272-6096. The examiner can normally be reached on Monday-Friday (9:00 AM-5:30 PM).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on (571)-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

  
Leslie A. Royds  
Patent Examiner  
Art Unit 1614

January 24, 2007

 1/27/07  
ARDIN H. MARSCHEL  
SUPERVISORY PATENT EXAMINER